#29 RD 11-7-02

DECLARATION OF CHRISTOPHER SOMERVILLE UNDER 37 C.F.R. § 1.132

Attorney Docket	2300-1481
First Named Inventor	Williams et al.
Application Number	09/297,648
Filing Date	March 10, 2000
Group Art Unit	1631
Examiner Name	J. Brusca
Title: *Human Genes and Gene Expression Products II*	

Dear Sir:

1. I, Christopher R. Somerville, declare and say I am a resident of the State of California. My residence address is 5 Valley Oak, Portola Valley, CA 94028.

2. I hold a B.Sc. degree in Mathematics, which I received from the University of Alberta, Canada in 1974. I further hold M.Sc. and Ph.D. degrees in Genetics, which I received from the University of Alberta, Canada in 1976 and 1978, respectively.

3. I am a Director of the Carnegie Institution of Washington Department of Plant Biology and a Professor of the Department of Biological Sciences at Stanford University. I am an elected member of the U.S. National Academy of Sciences, and an elected fellow of the Royal Societies of London and Canada. I serve on the editorial boards of several international peer-reviewed journals and have served on several panels for the NIH, NSF and USDA. I have worked in the field of recombinant DNA technology for over 20 years and have published over 150 articles in the fields of genetics, biochemistry, molecular biology and genomics (see curriculum vitae attached).

4. I have reviewed U.S. Patent Application No. 09/297,648 (hereinafter the '648 application), the first Office Action (specifically section No. 7) mailed November 29,

2000, the final Office Action (specifically section No. 12) mailed October 2, 2001, and the Advisory Action mailed May 31, 2002 in the '648 application.

5. I understand the inventions at issue (hereinafter "Inventions") are defined by the following claims:

Claims 146-148

Claim 146 is a formula in which the Invention is defined as a genus of polynucleotides characterized as having the common structural feature of a nucleotide sequence containing a minimum of 50 contiguous nucleotides of SEQ ID NO:253. I understand that the genus of polynucleotides defined by Claim 146 includes polynucleotides that contain additional sequences (i.e. flanking sequences) other than the specified contiguous region. Claim 147 defines the Invention as a vector containing the Invention of Claim 146, and Claim 148 defines the Invention as host cells containing the Invention of Claim 147.

Claims 149-150

Claim 149 is a formula in which the Invention is defined as a genus of polynucleotides characterized by the common structural feature of (1) a length that is a minimum of 50; and (2) sufficiently structural similarity to SEQ ID NO:253 to allow the polynucleotide to hybridize under stringent conditions to a polynucleotide having a sequence of SEQ ID NO:253. Claim 150 further defines the stringent conditions used for hybridization.

Claim 151

Claim 151 defines the Invention as a genus of polynucleotides characterized as containing a sequence that is the same as the sequence of an cDNA insert found in the clone number M00001448D:C09, deposited with the ATCC. I understand that the genus of polynucleotides defined by claim 151 includes polynucleotides that contain additional sequences (i.e. flanking sequences) other than that specified by SEQ ID NO:253.

Claims 152-154

Claim 152 defines the Invention as a genus of isolated polynucleotides characterized as having the common structural feature of a nucleotide sequence containing a minimum of 50 contiguous nucleotides of SEQ ID NO:253, obtained as a product of amplification using at least one oligonucleotide primer that contains at least 15 contiguous nucleotides of the sequence of SEQ ID NO:253. Claim 153 defines the Invention as a vector containing the Invention of Claim 152, and Claim 154 defines the Invention as host cells containing the Invention of Claim 153.

In this Declaration, I will be addressing these Inventions.

6. I have been asked to opine of the following questions:

a) Would one of ordinary skill in the art to which the Inventions pertain (hereinafter the "Skilled Person") would conclude from a review of the '648 application as a whole that the Inventions are described therein and the inventors were in possession of the Inventions?

b) Would the Skilled Person conclude from a review of the '648 application as a whole that the disclosures therein are representative of the genera defined by the Inventions?

It is my opinion, based on the facts and reasoning set forth below, that the answer to each of these questions is "yes."

Skilled Person

7. It is my understanding that the application is to be viewed from the standpoint of one of ordinary skill in the art in the relevant field at the time of filing of the application (referred to here as the "Skilled Person"). The '648 application was filed on March 10, 2000 and relates to the field of recombinant DNA technology. I would expect a Skilled Person in the field of recombinant DNA technology in March 2000 to

have been represented by a scientist with a Ph.D. degree and two years of post-doctoral training. I consider that such a Skilled Person would have the ability to analyze a DNA sequence using the common general knowledge, tools, and methods available in the field and without inventive effort. Furthermore, such a Skilled Person would have had access to and would have used as needed persons of ordinary skill in other technical fields, such as (by way of illustration and not limitation) cellular biology, oncology, biochemistry, immunology, physiology and diagnostics.

8. In March 2000, the common general knowledge, tools, and well-known methods available in this field were extensive. Widely available methods included nucleotide hybridization, nucleic acid cloning, polymerase chain reaction (PCR), reverse transcriptase PCR (RT-PCR), gene sequencing and cDNA library construction and screening. In addition, several "bioinformatics" tools were available, such as bioinformatics programs for searching a database of nucleic acids sequences for similar nucleic acid sequences (e.g. BLAST), programs for comparing two nucleic acid sequence (e.g. the BESTFIT or GAP programs as provided by the University of Wisconsin's GCG program) and programs for predicting and annotating coding sequences of genes (e.g. GENSCAN and XGRAIL).

9. Since I a) regularly attended external and internal meetings on molecular biology topics at which Skilled Persons presented their research, b) regularly read and reviewed scientific literature in which Skilled Persons presented their research, and c) was head of a laboratory in which several Skilled Persons have received training, prior to and during March 2000, I believe that I am qualified by training and experience to address what a Skilled Person would have understood from a reading of the specification of U.S. Patent Application No. 09/297,648 as of its filing date on March 10, 2000.

[redacted]

10. The following remarks constitute the basis for my opinion that the Skilled Person would conclude, from a review of the '648 application as a whole, that the Inventions were described in the '648 application and in the inventors' possession, and further that the disclosure of '648 application contains representative examples of the Inventions.

Claims 146-148

11. The specification describes the Inventions of Claims 146-148 in a number of passages, including the following:

In the sequence listing submitted as part of the application, SEQ ID NO:253 is provided as follows:

```
<400> 253
gaacaaagaa ggaatgtctt cctcatgttt gggtctatag aagacgttaa agaaaacttc   60
aagaaagtgg gtttgaggca tgagccacca cgcctggcca aaggatttaa tgaattaatg  120
gatgtacagt gctggggctg ttattctagg gcctgcattg agactcacat tttgccatca  180
aaagcctttt aagaggtgga ggttgcggtg agctgacatg gtgccactgc actccggcct  240
gagtgacaga gtgagactct gtctcacaaa aaaaataatg ccctttaaat aatgaataat  300
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An actual clone encompassing the sequence of SEQ ID NO:253 was deposited with the A.T.C.C. as clone number M00001448D:C09 of ATCC Deposit Number 207068.

On page 9, lines 6- 10 of the specification, particular lengths of regions of SEQ ID NO:253 are described:

> Isolated polynucleotides and polynucleotide fragments of the invention comprise at least about 10, about 15, about 20, about 35, about 50, about 100, about 150 to about 200, about 250 to about 300, or about 350 contiguous nucleotides selected from the polynucleotide sequences as shown in "SEQ ID NOS:1-5252."

[redacted]

Taking these disclosures together, the Skilled Person would find described in the '648 application all sequences of at least 50 contiguous polynucleotides contained within SEQ ID NO:253.

12. I am informed that in the language of patent law the term "comprise" as used in the above claims means that flanking sequences can be present in addition to the specified sequence. A genus of polynucleotides containing flanking regions is describe in the '648 application, as discussed further below.

13. Nucleic acid probes containing the specified sequence, which a Skilled Person would recognize as often longer than the specified sequence from the SEQ ID, are described in several positions in the specification, for example:

on page 9, lines 15-22:

> Probes specific to the polynucleotides of the invention can be generated using the polynucleotide sequences disclosed in "SEQ ID NOS:1-5252." The probes are preferably at least about 12, 15, 16, 18, 20, 22, 24, or 25 nucleotide fragment of a corresponding contiguous sequence of "SEQ ID NOS:1-5252", and can be less than 2, 1, 0.5, 0.1, or 0.05 kb in length. The probes can be synthesized chemically or can be generated from longer polynucleotides using restriction enzymes. The probes can be labeled, for example, with a radioactive, biotinylated, or fluorescent tag. Preferably, probes are designed based upon an identifying sequence of a polynucleotide of one of "SEQ ID NOS:1-5252."

and on page 10, lines 12-19:

> The subject nucleic acid compositions can be used to, for example, produce polypeptides, as probes for the detection of mRNA of the invention in biological samples (*e.g.*, extracts of human cells) to generate additional copies of the polynucleotides, to generate ribozymes or antisense oligonucleotides, and as single stranded DNA probes or as triple-strand forming oligonucleotides. The probes described herein can be used to, for example, determine the presence or absence of the polynucleotide sequences as shown in "SEQ ID

> NOS:1-5252" or variants thereof in a sample. These and other uses are described in more detail below.

Furthermore, Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 2nd Ed., (1989) Cold Spring Harbor Press, Cold Spring Harbor, NY., which is incorporated by reference into the application, discloses several types of probes that contain flanking sequences, including hybridization probes, oligonucleotide probes, RNA probes, plasmid probes and polymerase chain reaction probes. For example, a Skilled Person would recognize that a probe may contain polylinker sequences, or an oligonucleotide "tail". The Skilled Person would also know that much longer sequences, such as vectors containing the sequence specified from the SEQ ID can be used as probes.

14. Vectors containing the specified sequence, which a Skilled Person would recognize as always being longer than the specified sequence, are described in several positions in the specification. For example, on page 10, lines 3-6, that an Invention can be contained in a vector is recited:

> The polynucleotides of the invention can be provided as a linear molecule or within a circular molecule. They can be provided within autonomously replicating molecules (vectors) or within molecules without replication sequences. They can be regulated by their own or by other regulatory sequences, as is known in the art.

On page 15, lines 5-12, several types of vector, including expression vectors, viral vectors, non-viral vectors and plasmids are described:

> Appropriate polynucleotide constructs are purified using standard recombinant DNA techniques as described in, for example, Sambrook *et al., Molecular Cloning: A Laboratory Manual, 2nd Ed.*, (1989) Cold Spring Harbor Press, Cold Spring Harbor, NY, and under current regulations described in United States Dept. of HHS, National Institute of Health (NIH) Guidelines for Recombinant DNA Research. The gene product encoded by a polynucleotide of the invention is

> expressed in any expression system, including, for example, bacterial, yeast, insect, amphibian and mammalian systems. Suitable vectors and host cells are described in U.S. Patent No. 5,654,173.

And on page 16, lines 16-23, several more vectors are described:

> Polynucleotide molecules comprising a polynucleotide sequence provided herein propagated by placing the molecule in a vector. Viral and non-viral vectors are used, including plasmids. The choice of plasmid will depend on the type of cell in which propagation is desired and the purpose of propagation. Certain vectors are useful for amplifying and making large amounts of the desired DNA sequence. Other vectors are suitable for expression in cells in culture. Still other vectors are suitable for transfer and expression in cells in a whole animal or person. The choice of appropriate vector is well within the skill of the art. Many such vectors are available commercially.

And numerous examples of types of retroviral vectors, alphaviral vectors, adeno-associated viral vectors and adenoviral vectors are described in the specification on page 74, line 13 to page 75, line 19.

15. On page 8 lines 16-21 of the specification, cDNA polynucleotides containing the specified sequence, which a Skilled Person would recognize as longer than the specified sequence, are described:

> The term "cDNA" as used herein is intended to include all nucleic acids that share the arrangement of sequence elements found in native mature mRNA species, where sequence elements are exons and 3' and 5' non-coding regions. Normally mRNA species have contiguous exons, with the intervening introns, when present, being removed by nuclear RNA splicing, to create a continuous open reading frame encoding a polypeptide of the invention..

Furthermore, the actual vector encompassing the sequence of SEQ ID NO:253 was deposited with the A.T.C.C. is a cDNA clone.

16. Finally, on page 8, line 13 to page 9 line 2, the specification discloses a gene containing the specified sequence, which a Skilled Person would recognize as longer than the specified sequence, is described:

> The subject nucleic acids can be cDNAs or genomic DNAs, as well as fragments thereof, particularly fragments that encode a biologically active gene product .....
>
> A genomic sequence of interest comprises the nucleic acid present between the initiation codon and the stop codon, as defined in the listed sequences, including all of the introns that are normally present in a native chromosome. It can further include the 3' and 5' untranslated regions found in the mature mRNA. It can further include specific transcriptional and translational regulatory sequences, such as promoters, enhancers, *etc.*, including about 1 kb, but possibly more, of flanking genomic DNA at either the 5' and 3' end of the transcribed region. The genomic DNA can be isolated as a fragment of 100 kbp or smaller; and substantially free of flanking chromosomal sequence. The genomic DNA flanking the coding region, either 3', and 5', or internal regulatory sequences as sometimes found in introns, contains sequences required for proper tissue, stage-specific, or disease-state specific expression.

17. In summary, the '648 specification specifically describes the sequence of SEQ ID NO:253 and the '648 specification specifically describes polynucleotides containing at least 50 contiguous nucleotides of SEQ ID NO:253. The '648 specification also specifically describes a wide variety of polynucleotides containing at least 50 contiguous nucleotides of SEQ ID NO:253 along with flanking sequences, e.g. probes, vectors, cDNAs, clones, full length cDNAs, genes etc. As such the '648 specification describes large polynucleotides containing fragments of SEQ ID NO:253 that are, for example, useful as probes or starting materials for probes (see, e.g., page 5, lines 7-14 of the '648 specification). The vector containing a cDNA containing the sequence of SEQ ID NO:253 and deposited with the A.T.C.C. is an example of a polynucleotide containing SEQ ID NO:253 and having such flanking sequences. The overall disclosure of the specification demonstrates that there is no criticality to sequences flanking the polynucleotides of the Invention. Rather, selection of such

flanking sequences is an arbitrary matter of design. The Skilled Person would readily appreciate from the specification that the sequence of SEQ ID NO:253 can be incorporated within a vast number of larger polynucleotides, and that each of these sequences is identifiable as having at least 50 contiguous nucleotides of SEQ ID NO:253.

18. When read in conjunction with the '648 specification, it is my unequivocal opinion that, a Skilled Person would find that the '648 specification describes polynucleotides fully representative of the genus of polynucleotides of the Invention since

a) the Skilled Person would recognize disclosure of SEQ ID NO:253 as fully representative of the genus of the Invention since it is a complete disclosure of the common structural feature (i.e., at least 50 contiguous nucleotides of SEQ ID NO:253) of the Inventions; and

b) the Skilled Person would recognize the vector containing a cDNA containing the sequence of SEQ ID NO:253 and deposited with the A.T.C.C. is an example of a polynucleotide containing SEQ ID NO:253 having flanking sequences and as being fully representative of large polynucleotides that can serve as probes or starting materials for probes in cancer diagnostics.

19. Based upon the above, the Skilled Person would conclude that the specification substantially and in detail describes the genus of polynucleotides encompassed in these claims 146-148. It is therefore my unequivocal opinion that a Skilled Person would, in March 2000, thus would find a clear and unambiguous description of the Inventions in Claims 146-148. Based on the foregoing, it is also my unequivocal opinion that a Skilled Person would find that the '648 specification demonstrates that applicants had possession of the genera of polynucleotides of claims 146-148.

[redacted]

20. Furthermore, a Skilled Person, by performing a simple sequence comparison, e.g. a pairwise "BESTFIT" alignment between SEQ ID NO:253 and any given nucleotide would have been able to straightforwardly determine whether a given polynucleotide fell within any one of the claims: the given polynucleotide either has 50 nucleotides of sequence identity with SEQ ID NO:253 or it does not.

Claims 149-150

21. I shall now address the Invention of Claims 149-150. In addition to the above-described portions of the specification and information known to the Skilled Person, I rely on the following in forming my opinion. .

22. Page 6 lines 2-28 of the specification describes a genus of polynucleotides that hybridize under stringent conditions to a polynucleotide having a sequence provided by the sequence listing:

> The polynucleotides of the invention also include polynucleotides having sequence similarity or sequence identity. Nucleic acids having sequence similarity are detected by hybridization under low stringency conditions, for example, at 50°C and 10XSSC (0.9 M saline/0.09 M sodium citrate) and remain bound when subjected to washing at 55°C in 1XSSC. Sequence identity can be determined by hybridization under stringent conditions, for example, at 50°C or higher and 0.1XSSC (9 mM saline/0.9 mM sodium citrate). Hybridization methods and conditions are well known in the art, see, *e.g.*, U.S. Patent No. 5,707,829.

23. The specification, on page 6 line 28 to page 7 line 3 further describes that the Inventions may be allelic variants, cDNAs or genes, and may be from a variety of species, including humans.

> Nucleic acids that are substantially identical to the provided polynucleotide sequences, *e.g.* allelic variants, genetically altered versions of the gene, *etc.*, bind to the provided polynucleotide sequences ("SEQ ID NOS:1-5252") under stringent hybridization

> conditions. By using probes, particularly labeled probes of DNA sequences, one can isolate homologous or related genes. The source of homologous genes can be any species, *e.g.* primate species, particularly human; rodents, such as rats and mice; canines, felines, bovines, ovines, equines, yeast, nematodes, etc.
>
> Preferably, hybridization is performed using at least 15 contiguous nucleotides of at least one of "SEQ ID NOS:1-5252." That is, when at least 15 contiguous nucleotides of one of the disclosed SEQ ID NOs. is used as a probe, the probe will preferentially hybridize with a gene or mRNA (of the biological material) comprising the complementary sequence, allowing the identification and retrieval of the nucleic acids of the biological material that uniquely hybridize to the selected probe. Probes from more than one SEQ ID NO. will hybridize with the same gene or mRNA if the cDNA from which they were derived corresponds to one mRNA. Probes of more than 15 nucleotides can be used, but 15 nucleotides represents enough sequence for unique identification.

24. It is well established that, in order to hybridize, two polynucleotides must share a definable structural characteristic: a region of significant sequence identity. The structural characteristic that defines the claimed genus is SEQ ID NO:253, to which members of the group hybridize under stringent conditions. Some of the polynucleotides encompassed by the claim may be longer than the sequence of SEQ ID NO:253 and contain flanking sequences, however, since they must be able to hybridize with a specified polynucleotide they must have sequences that are similar to the sequence of the specified polynucleotide, and thus are limited in structure by this requirement. As such, the structural characteristic defining this genus of claimed sequences is the sequence of SEQ ID NO:253.

25. I have also reviewed the U.S. Patent & Trademark Office's "Synopsis of Application of Written Description Guidelines,", as posted to the U.S.P.T.O world wide website on March 1, 2000 and I agree with the assertion that "a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claim because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs", as recited on page 36. I also agree with the

Synopsis of Application of Written Description Guidelines in that a recitation of "hybridization" in a claim imposes a structural limitation onto the claimed Inventions.

26. It is therefore my unequivocal opinion that a Skilled Person would, in March 2000, have found the specific description of the claimed genus of polynucleotides in the specification to be a sufficient structural description of the claimed Inventions and to demonstrate applicants had possession of the Invention of Claims 149 or 150.

27. Furthermore, the Skilled Person would have been able to straightforwardly determine whether a given polynucleotide falls within Claims 149 or 150 by performing a straightforward stringent hybridization experiment, or by calculating the Tm of the a hybrid polynucleotide molecule under certain hybridization conditions using the well known equation provided by Sambrook et al (Molecular Cloning: A Laboratory Manual, CSHL Press, 1989).

"Tm = 81.5 + 1.6(log10[Na+]) + 0.41(fraction G + C)
– 0.63(% formamide) – (600/length of probe)"

Claim 151

28. I will now discuss the Invention of Claim 151. In addition to the above-described portions of the specification and information known to the Skilled Person, I rely on the following in forming my opinion.

29. Table 1 of the '648 application describes biological deposits which include vectors containing an insert, which insert contains the sequences described in the application. Table 1 indicates that a clone encompassing the sequence of SEQ ID NO:253 is deposited as clone M00001448D:C09 of Deposit Number 207068at the ATCC.

30. SEQ ID NO:253 represents a part of the nucleotide sequence contained within the insert of the deposited clone, and, as such, the deposited clone contains an

polynucleotide insert that is longer than SEQ ID NO:253 and contains flanking sequences. Since the deposited clone is from a library made from mRNA, the flanking sequence are cDNA flanking sequences.

31. Based upon the above disclosures in the '648 application, it is my unequivocal opinion that a Skilled Person would find that the '648 application describes the Invention of Claim 151 and recognize that the inventors were in possession of that Invention.

Claims 152-154

32. I will now discuss the Invention of Claims 152-154. In addition to the above-described portions of the specification and other information known to the Skilled Person, I rely on the following in forming my opinion.

33. Amplification is a process for synthesizing a nucleic acid enzymatically. To perform amplification, at least one oligonucleotide probe (i.e. a primer of a defined sequence) hybridizes with (i.e. base pairs to) a template nucleic acid (i.e., the starting material), and the probe is enzymatically extended to form a copy of one strand of the nucleic acid. Subsequent extension steps amplify both strands of the nucleic acid to form a duplex nucleic acid product that contains at least the probe binding site. Probe binding sites are usually at least 12-15 nucleic acids in length, and, as such, both the amplification product and the probes share a sequence of at least 12-15 nucleotides.

34. Amplification strategies, such as the polymerase chain reaction (PCR), lockdown PCR, and rapid amplification of cDNA ends (RACE) were well understood and practiced a Skilled Person in March 2000 (e.g. as described by the laboratory manuals Ausubel et al. (*Short Protocols in Molecular Biology*, 3rd ed., Wiley & Sons, 1995 and Sambrook et al., (*Molecular Cloning: A Laboratory Manual*, Second Edition,

1989 Cold Spring Harbor, N.Y.). In many amplification strategies, such as RACE and lockdown PCR, nucleotide sequences flanking a sequence of interest may be amplified. In the specification, several amplification strategies are detailed, such as PCR, lockdown PCR and RACE. In most PCR methods, probes are first designed, and the PCR is performed. The specification provides description of a SEQ ID NO:253, a description of probes, and a description of PCR methods as follows:

35. SEQ ID NO:253 is described in the sequence listing submitted as part of the application, as recited in paragraph 11, *supra.*

36. Probe sequences are detailed in the specification on page 9, lines 15-18:

> Probes specific to the polynucleotides of the invention can be generated using the polynucleotide sequences disclosed in "SEQ ID NOS:1-5252." The probes are preferably at least about 12, 15, 16, 18, 20, 22, 24, or 25 nucleotide fragment of a corresponding contiguous sequence of "SEQ ID NOS:1-5252",

37. Polymerase Chain Reaction (PCR) is detailed in the specification at page 37, lines 1-6.

> The Polymerase Chain Reaction (PCR) is another means for detecting small amounts of target nucleic acids (see, *e.g.*, Mullis *et al.*, *Meth. Enzymol.* (1987) *155*:335; U.S. Patent No. 4,683,195; and U.S. Patent No. 4,683,202). Two primer polynucleotides nucleotides hybridize with the target nucleic acids and are used to prime the reaction. The primers can be composed of sequence within or 3' and 5' to the polynucleotides of the Sequence Listing.

38. On page 13, lines 4-15, RACE is described:

> "Rapid amplification of cDNA ends," or RACE, is a PCR method of amplifying cDNAs from a number of different RNAs. The cDNAs are ligated to an oligonucleotide linker, and amplified by PCR using two primers. One primer is based on sequence from the instant polynucleotides, for which full length sequence is desired, and a

> second primer comprises sequence that hybridizes to the oligonucleotide linker to amplify the cDNA. A description of this methods is reported in WO 97/19110. In preferred embodiments of RACE, a common primer is designed to anneal to an arbitrary adaptor sequence ligated to cDNA ends (Apte and Siebert, *Biotechniques* (1993) *15*:890-893; Edwards *et al.*, *Nuc. Acids Res.* (1991) *19*:5227-5232). When a single gene-specific RACE primer is paired with the common primer, preferential amplification of sequences between the single gene specific primer and the common primer occurs. Commercial cDNA pools modified for use in RACE are available.

39. On page 13, lines 16-18, an anchored PCR strategy is described:

> Another PCR-based method generates full-length cDNA library with anchored ends without needing specific knowledge of the cDNA sequence. This method is described in WO 96/40998.

40. In summary, the specification specifically describes SEQ ID NO:253, the specification specifically describes that oligonucleotide probes for use in amplification can be at least 15 contiguous nucleotides of an SEQ ID NO:253, and the specification specifically describes starting material for use in the amplification process, as well as the polynucleotides that would be produced by amplification using the probes and the starting material. These polynucleotides share the structural feature of at least 50 contiguous nucleotides of SEQ ID NO:253.

41. Based upon the above disclosures in the '648 application, it is my unequivocal opinion that a Skilled Person would find that the '648 application describes the Invention of Claims 152-154 and recognize that the inventors were in possession of that Invention

The Office Actions

42. I have been asked to comment on the Office Actions, including the first Office Action (specifically section No. 7) mailed November 29, 2000 and the final Office Action (specifically section No. 12) mailed October 2, 2001.

43. It is my understanding that the positions outlined in these Office Actions were taken with respect to other claimed Inventions, and that the same reasoning might be applied to the new claims directed to these Inventions.

44. As I understand it, claims directed to the above-described Inventions have been rejected as containing subject matter which was not described in the specification in such a way as to reasonably convey to one of ordinary skill in the art that the Inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Office Action argues that the specification provides insufficient written description to support the genus of nucleic acid sequences encompassed by the claims, which include sequences longer than SEQ ID NO:253 and sequences that hybridize to SEQ ID NO:253. The Office Actions further asserts that with the exception of a polynucleotide that is limited to at least 50 contiguous nucleotides of SEQ ID NO:253 and no more, one of ordinary skill in the art cannot envision the detailed chemical structure of the encompassed polynucleotides, regardless of the complexity or simplicity of the method of isolation. Based on my knowledge of the Skilled Person, I disagree with this statement.

45. As I have discussed above, the sequence of SEQ ID NO:253 defines structural features commonly possessed by members of each of the genera of the Inventions that distinguish them from other polynucleotides. SEQ ID NO:253 thus defines the claimed genera of polynucleotides such that a Skilled Person would have recognized that the inventors had possession of and had invented the claimed polynucleotides.

[redacted]

Moreover, the Skilled Person would have been able to straightforwardly determine whether a given polynucleotide falls within any one of the claims based on the provided structural characteristics or routine hybridization experiments. Only routine methodologies would be required to determine whether a given polynucleotide would be within a genus of an Invention. The specification provides, therefore, sufficient written description of the characterizing details sufficient to distinguish the claimed genera of polynucleotides from all others, which means the genera are readily recognizable by the Skilled Person.

46. Furthermore, in reviewing the Office Actions, I note that the written description rejection cites the following court decisions in support of the rejection: *Amgen, Inc. v. Chugai Pharmaceutical Co.*, *Fiers v. Revel*, *Fiddes v. Baird*, and *University of California v. Eli Lilly and Co.* I understand that the disputed patent applications were filed in the between the late 1970's and the mid-1980s.

47. Since the field of recombinant DNA technology is a rapidly evolving, and most major technological advances have been made in the last 20 years (e.g. computer programs for comparing nucleic acids), a Skilled Person had a dramatically higher skill level in March 2000 as compared to the filing dates of the applications involved in the above court decisions. As I understand it, the written description requirement is evaluated in the context of the person of ordinary skill in the art at the time of filing. Because of the advances in the art, I do not believe that a statement regarding what one of ordinary skill can or cannot do in the above cases could be evidence with respect to what the Skilled Person in March of 2000 could or could not do.

48. I, Christopher R. Somerville, hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge

that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title XVIII of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

11-1-02
Date

Christopher R. Somerville, Ph.D.

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CURRICULUM VITAE

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Home: 5 Valley Oak, Portola Valley, CA 94028

Birthdate: October 11, 1947

Citizenship: USA (Naturalized 2/28/95)

Education:

Ph.D. (genetics), 1978, University of Alberta, *E. coli* mutants defective in pppGpp hydrolysis
M.Sc. (genetics), 1976, University of Alberta, Positive gene regulation by *relA* in *E. coli*
B.Sc. (mathematics), 1974, University of Alberta

Employment:

Director, Carnegie Institution of Washington Department of Plant Biology, 1994-
Professor, Department of Biological Sciences, Stanford University, 1994-
Professor, Department of Botany and Plant Pathology and MSU-DOE Plant Research Laboratory, Michigan State University, 1986-93
Associate Professor, MSU-DOE Plant Research laboratory, Michigan State University, 1982-86
Assistant Professor, Department of Genetics, University of Alberta, 1981 -82
Research Associate, Department of Agronomy, University of Illinois 1978-81

Awards:

Kuhmo Award (2001); D.Sc., Wageningen University (1998);
Visiting Professor, University of Glasgow (1998-);
D.Sc., University of Alberta (1997);
Elected to U.S. National Academy of Sciences (1996);
D.Sc., Queens University (1993);
American Society of Plant Physiologists Gibbs Medal (1993);
Elected Fellow of Royal Society of Canada (1993);
Humbolt Senior Research Award (1992);
MSU Distinguished Faculty Award (1992);
Elected Fellow of Royal Society London (1991);
Schull Award, American Society of Plant Physiologists (1987);